

**REMARKS**

Applicant respectfully requests favorable reconsideration of this application.

Claims 70, 72–75, 77, 78, and 92–96 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Northrup (US 5,639,423) in view of Gravlee (US 3,961,097) and in further view of Ishibashi (US 5,984,881), while Claims 79 and 98–104 were rejected as being unpatentable over Northrup in view of Gravlee and Ishibashi, and in further view of Vago (US 5,665,141). Applicant respectfully traverses.

The Office Action notes that Northrup discloses a transducer that produces Lamb waves with frequencies from 1 to 200 MHz, and alleges that Northrup therefore anticipates the claimed frequency of “at least 100 KHz.” *See*, Office Action at Page 8 (Paragraph 22).<sup>1</sup> Applicant disagrees. At most, Northrup discloses a minimum frequency of 1 MHz (i.e., 1,000 kHz), and Applicant submits that Northrup fails to teach or suggest that a frequency lower than 1,000 kHz can be used. *See*, Col. 11:4–6 (“The Lamb waves in this invention have frequencies in the approximate range of 1 to 200 MHz ...” emphasis added). Consequently, Northrup fails to disclose the claimed frequency of “at least 100 KHz,” as recited by Claims 77 and 98, and Applicant submits that these claims are allowable at least for this reason.

New Claims 105 and 106 recite an ultrasound frequency range of 100 KHz to 1 MHz. Support for this subject matter may be found, for example, in the Specification on Page 10, line 18 (“0.1 to 1 MHz ...”), Page 13, line 11 (“a frequency in the range of 0.1 to 1 MHz can be used ...”), etc. No new matter has been added, and Applicant submits that none of the cited references teaches or suggests this ultrasound frequency range. Consequently, Claims 105 and 106 are allowable, at least for this reason.

**Claims 70 and 98 Are Allowable Over the Cited References**

Applicant respectfully submits that the Office Action has failed to establish a *prima facie* case of obviousness against Claims 70 and 98 for several reasons. *See*, e.g., MPEP § 2143.

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<sup>1</sup> *See*, Office Action at Page 22, Paragraph 22 (“Since the limitation at least 100 KHz would indicate any frequency greater than or equal to 100 KHz, the limitation is anticipated, and applicant’s argument is not found persuasive”).

Fundamentally, none of the cited references teaches or suggests a central processor that controls an ultra sound generator to fix a tissue sample in a solution with no or minimal damage. Notwithstanding this deficiency, there is simply no teaching or suggestion that supports the combination of these references, as alleged by the Office Action. *See*, Office Action at Pages 3–5.

Northrup discloses an integrated microfabricated instrument for the manipulation, reaction and detection of microliter to picoliter samples for DNA-based reactions, such as the polymerase chain reaction (or PCR). Northrup teaches that the small size of his reaction chamber facilitates rapid thermal cycling, and that Lamb-wave devices may be used as sensors, pumps and agitators. *See*, e.g., Abstract; Col. 3:39–49; Col. 4:49–65; Col. 7:29–31, 35–41, 61–62; Col. 8:20–23; etc. Northrup generally teaches that ultrasonic waves are used to manipulate cells and cell-contents “by stirring and or mixing reagents from other chambers on the microinstrument” (Col. 5:42–52). During the PCR reaction, Northrup specifically discloses that his Lamb-wave transducer,  $LW_C$ , is used as an “agitator or mixer as described below to mix the reagents and promote the reaction” within reaction chamber 30 (Col. 8:21–23). Thus, Northrup teaches that his Lamb-wave transducer  $LW_C$  agitates or mixes the contents of reaction chamber 30 during a particular reaction.

Northrup fails to teach or suggest a reaction chamber that includes a solution for fixing a tissue sample placed therein, and a central processing unit, coupled to the ultrasound generator and the sensor, to control the ultrasound generator by adjusting at least one of a frequency and an intensity of the ultrasound energy, in response to a signal received from the sensor, to fix the tissue sample in the solution with no or minimal damage, as recited by Claims 70 and 98. The Office Action admits these deficiencies, and cites Gravlee and Ishibashi in support of its obviousness rejection. *See*, Office Action at Pages 3–5.

Neither Gravlee nor Ishibashi disclose a central processing unit to control the ultrasound generator to fix the sample in the solution with no or minimal damage, as recited by Claims 70 and 98. Instead, Gravlee merely discloses that “ultrasound energy” may be used to reduce the time required to process a tissue specimen, preferably contained within a “relatively small vessel,” for microscopic examination. *See*, e.g., Col. 1:65 to Col. 2:17, etc. Ishibashi discloses

an ultrasonic therapeutic apparatus, used to treat cancerous tissue, that includes a computer 223 that controls "a power supply 229 for driving the [ultrasonic] applicator 226" (Col. 25:50–51). Consequently, Applicants submit that none of the cited references teaches or suggests a central processing unit to control an ultrasound generator to fix the sample in a solution with no or minimal damage, as recited by Claims 70 and 98.

Notwithstanding the failure of the cited references to disclose all of the features recited by Claims 70 and 98, the Office Action also fails to establish why one of ordinary skill in the art would combine the teachings of these disparate references. Northrup discloses that the purpose of his sonication is to disrupt and expose cell components through lysis, which are then used by subsequent processes. *See, e.g.,* Col. 5:44–47, 52–57, 57–61. In other words, Northrup teaches that this pre-PCR use of ultrasound leads to the destruction of his samples rather than their preservation.<sup>2</sup> Similarly, Ishibashi's "therapeutic ultrasonic waves are generated continuously ... thereby heating and necrotizing an abnormal tissue such as cancer" (Col. 10:30–34), which, of course, results in the destruction of the abnormal tissue. To the contrary, Gravlee discloses that the intensity of his ultrasonic energy "must be maintained at a level below the level at which damage to cells in the tissue occurs" (Col. 3:50–52). Accordingly, Applicant submits that one of ordinary skill in the art would not combine these references due to their inapposite purposes, i.e., the destruction of tissue (Northrup and Ishibashi) as compared to its preservation (Gravlee). Consequently, the Office Action has failed to establish a *prima facie* case of obviousness, and Applicants suspect that the Office Action is engaging in impermissible hindsight reconstruction in order to arrive at the claimed invention.

Accordingly, Claims 70 and 98 are allowable over the cited references. Claims 72–75, 77–79, 92–96 and 105, depending from Claim 70, and Claims 99–104 and 106, depending from Claim 98, are also allowable, at least for the reasons discussed above.

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<sup>2</sup> The instant application seeks to preserve the morphology of samples, for subsequent processes, in order to provide information about proteins and nucleic acids, as well as the histological appearance of the tissue sample. Indeed, Northrup's "subsequent techniques," discussed, for example, at Col. 6:1-10, do not involve any quality of the sample other than the extracted DNA.

In view of the amendments and remarks presented herein, Applicant respectfully submits that this application is in condition for allowance and should now be passed to issue. Reconsideration and early Notice of Allowance is requested.

Respectfully submitted,  
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